SOME CLINICAL OBSERVATIONS

on

TRYPANOSOMIASIS RHODESIENSIS.

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I. INTRODUCTORY.

TRYPANOSOMIASIS RHODESIENSIS or Rhodesian Sleeping Sickness was first described as a distinct variety of human trypanosomiasis in 1910. At that time it was known to be endemic in Rhodesia and Nyassaland, in 1912 and 1913 its occurrence was noted in the southern part of Tanganyika Territory and in Portuguese East Africa, and cases have since been reported as far North as the Southern Soudan.

Until very recent years it was considered to be purely an endemic disease but a most important stage in its history was reached when, in 1922, a localised outbreak which rapidly assumed epidemic proportions took place in the Mwanza Province of Tanganyika Territory. This outbreak was of great interest, not only because it was the first great epidemic of Rhodesian Sleeping Sickness to be recorded, but because the infecting trypanosome was found to be conveyed by a new insect vector, Glossina swynnertoni, and direct transmission from man to man was the main, if not the only, means of spread. In 1924 another epidemic, spread by G.morsitans, was reported in the Ufipa District of the same Territory and the disease now appears to be established in epidemic form.

Since the very early days of white colonization in Africa, the tsetse fly and the diseases of man and beast that follow in the train of that insect pest have been the scourge of the continent, and the

intention of the writer to attempt to draw a complete clinical picture, but rather to place on record points of importance and interest personally observed and recorded during the study of a series of 94 consecutive cases, particular attention being paid to the action of the more recent drugs, and to the diagnostic value of early symptoms and special features in atypical cases.

The extensive subject of the epidemiology of trypanosomiasis with its associated entymological and protozoological problems, and the possibilities and relative merits of various prophylactic measures, do not come within the scope of this paper, and can only be lightly touched upon. The conditions under which the work was done made detailed scientific and laboratory investigations impossible.

(c) Nature of the Country :-

The observations were made in the Ufipa District of Tanganyika Territory (Long 32°E., Lat. 7°S.) in the southern part of the main Ufipa/Tabora epidemic area. The country included the flat, low-lying, thorn acacia forests of the Rukwa Valley, and, outside the Valley, the more hilly and lighter 'Miombo' and 'Mininga' bush. The whole area is part of the great fly-belt which extends southwards from the Central Railway and involves upwards of 40,000 square miles of territory.

The natives are divided up into small and back-

backward tribes, and they live scattered about in small, isolated villages in the forest. Their deitary is based on maize, millets, beans, and sweet potatoes, supplemented by fish and occasionally by game meat. Fish and bees wax are the only commercial products, a few goats and sheep exist in the larger settlements, but cattle cannot live.

G.morsitans was the only variety of tsetse fly encountered, and the whole country was thickly stocked with game of all kinds.

(d) General Measures and Conditions :-

The problem presented by an epidemic of Rhodesian Sleeping Sickness occurring in a vast area infested with G.moristans was a peculiarly difficult one. The measures taken to deal with the situation cannot be described in full, but, briefly outlined, they consisted in the withdrawal of the natives from the infected districts for concentration in settlements which had been made fly-free by clearing and were maintained in that condition by native cultivation. It was in one of these settlements, Rungwa, in the Rukwa Valley, 15 square miles in extent and populated by 5500 souls, that the majority of the 94 cases in the series under review were diagnosed, treated, and observed.

The conditions under which the work was done can only be described as primitive. There was no

white colonization in the area; there was a small District Station on the Fipa plateau five days march away, and stores and supplies were brought by head transport from Tabora, on the Central Railway, more than 200 miles from the main treatment centre.

In this centre at Rungwa successive years saw the gradual development of the 'hospital' from a collection of hastily erected native huts to a reasonably permanent mud and wattle structure. The medical staff consisted of one European Medical Officer, one fully trained native dispenser, and three native dressers. All kinds of medical work were undertaken as far as facilities permitted, in order to encourage the attendance of the natives, gain their confidence, and so increase the chance of early diagnosis. It was in order to preserve this confidence that examinations of the cerebro-spinal fluid were not performed with the regularity which is really necessary in any full investigation of Sleeping Sickness; a primitive native when sick may attribute physical improvement to a painful procedure, but after treatment, when relatively fit, he does not appreciate the value of lumbar punctures.

(e) Diagnosis :-

The original diagnosis of the type of trypanosomiasis in the epidemic was based upon the general features of cases and the fact that the

spread was by G.morsitans. The identity of the infecting trypanosome was then established by the finding of posterior nucleated forms in the blood of a black rat experimentally infected with blood from a typical case.

During subsequent investigations, diagnosis of individual cases was made by the demonstration of the trypanosomes in the blood, gland-juice, or cerebro-spinal fluid ; and no case was included in the series until that had been done.

(f) Acknowledgments :-

The whole work was done under the direction of Dr J. O. Shircore, C.M.G., Director of Medical and Sanitary Services, Tanganyika Territory, and Dr G. Maclean, Sleeping Sickness Officer Tanganyika Territory, and to them the writer owes his thanks for permission to use the cases observed for the purpose of this paper.

II. EPIDEMIOLOGY.

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(a) General Aspects :-

The main epidemiological aspects of the Ufipa epidemic have been described by MACLEAN (1926). The observer, carefully tracing the history of the epidemic spread as the bewildered natives had fled before the menace, established the fact that whatever might have been the cause of the original conflagration the main source of subsequent spread was direct man-fly-man transmission. Later, during and after the concentration of the natives, the writer had many opportunities of investigating the source of infections, and again a definite history of contact with a sick person could be obtained in many, though not every, case. After concentration had been completed movements of the natives from the settlements into the depopulated forest still resulted in fresh infections, but whether the origin of these will be found to be foci of infected 'fly' existing on main routes and in deserted villages or whether there really is an animal reservoir remains at present one of the problems in epidemiology.

(d) Trypanosomes in Game :-

With the object of ascertaining the trypanosome infection rate of the wild game in the epidemic area examinations were made of the bloods of 150 animals shot in the vicinity of the settlements.

For the examinations thick drop preparations of the peripheral blood stained by 'Giemsa' were used, a method which did not allow of the accurate classification of the trypanosomes in every case, but which was convenient and demonstrated comparatively light infections.

Full details of the results obtained are given in Appendix 'C'. Summarizing these, it was found that trypanosomes were present in 31 (20.6%) of the bloods examined and in 18 (58%)of the positives) the infection was probably T.brucei. The relatively high percentage of positive results is due to the large number of Waterbuck included in the series, over 50% of these animals being found positive by this simple test; and until the vexed question of identity of trypanosomes is settled this will remain a point of importance, as waterbuck were among the antelope most constantly found close to the settlements.

The above results agree in the main with those of more detailed investigations on the same subject made by KINGHORN and MONTGOMERY (1909); KINGHORN (1912); BRUCE, HARVEY, HAMERTON, DAVEY and BRUCE (1923); STOHR (1913) DUKE (1913); BRUCE, HAMERTON, WATSON and BRUCE (1914).

(c) Sex and Age Incidence:-

The following figures representing all

the cases in this series show that young children were not entirely immune, and that the heaviest incidence was among males at the age when exposure was likely to be greatest :-

TABLE I.

Sex and Age Incidence.

	Under 1 year.	1 - 10 years	10 - 15 years.	15-20 years	20-30 years	30-40 years	Over 40 years	Totals
Male	1	2	5	8	23	19	18	76
Female	-	-	2	3	4	6	3	18
Totals	1	2	7	11	27	25	21	95

III. INCUBATION PERIOD.

The incubation period of trypanosome infections in man is notably difficult to estimate as it is quite impossible, in the vast majority of cases, to ascertain the date of the infecting bite with any degree of certainty. The personal experience of the writer is that when the relative significance of a number of bites has to be considered little can be deduced from their individual severity or from the reaction they produce. In natives it is frankly impossible to obtain any history whatsoever as tsetse bites are incidental in their lives and the most severe will not be memorised by any lasting impression; and as regards Europeans it is doubtful if there is any evidence to show that an infecting bite causes more disturbance than that from a perfectly clean fly. Some bites are acutely painful but the discomfort is momentary; others produce wheals with local erythema and temporary irritation; and at times the only indication there is that a meal has been provided is the detection of a fully gorged insect upon the skin: all these can occur with great regularity and yet produce no sign of a successful or aborted infection.

So far the incubation period has not been worked out by conclusive experiment on the human subject, and our knowledge at present is gained from the consideration of suitable cases with a known period of exposure. The following are some such cases

are some such cases previously reported:- MURRAY 1912, 1 week or less; SANDERSON 1912, maximum 21 days, Europeans 7 - 14 days; NEWHAM 1919, 5 - 14 days; KINGHORN 1925 1 - 2 weeks; MACLEAN 1926 (1) native under 14 days, and MACLEAN 1926 (2) possible maximum 27 days, probable maximum 18 days.

In the series under review there are two cases where the onset of symptoms took place in a fly-free area after a definite period of exposure in an area known to be infected; both had been working at the coast for two years previously to the journey which involved passing through the infected belt, and neither had any history of previous illness. In one (Case 305) the incubation period can be placed at between 2 - 8 days, and in the other (Case (302) at between 4 - 17 days. There was no other opportunity for accurate estimation, but the writer has constantly found in the investigation of histories that an incubation of from 2 - 21 days accounted for an infection from a known source, a fact which, though perhaps not admissable as evidence, is suggestive and to a certain extent confirmatory.

In the foregoing paragraphs the term 'Incubation Period' has been assumed to mean the period elapsing between the date of the infecting bite and the onset of symptoms. So defined its estimation is complicated by the occurrence of cases where a peripheral blood infection exists without causing symptoms ; that subject has not been fully investigated, and the most definite statement that can be made from the

existing evidence is that the incubation period is commonly somewhere between 1 - 3 weeks.

IV. SYMPTOMATOLOGY.

(a) Onset :-

The initial symptoms in Trypanosomiasis Rhodesiensis vary within wide limits and the cases can only be broadly classified as regards onset into the two main types acute, and gradual.

In the acute type, which occurred in 24.4% of this series, the initial symptom was usually headache. This came on suddenly in a person apparently fit, and it was accompanied by shivering and other signs of sharp fever. In most cases there was a history of onset in the late afternoon or evening, after the daily work or an excursion involving strain and exposure to the sun, and the patient became definitely ill immediately. Pains in the limbs and general aches were common, and if these were a marked feature the whole condition closely resembled that seen in influenza, and allied conditions.

Acute onset with uncommon features was noted in three cases; in one there was a sudden fainting fit during the night and the patient lapsed at once into a stuporose condition; an acute, unilateral,

cervical adenitis was the first sign in another ; and the third was suddenly prostrated by severe pains in the legs accompanied by fever but no headache.

In the majority of cases (75.6%) there was no sudden crisis in the course of the trypanosome infection which percipitated the patient from health to sickness, and symptoms came on insidiously. Some degree of pyrexia was probably present in these cases, but a history of fever was seldom given.

Of the actual initial symptoms in this type headahce was the most common and occurred in 41.5% of the total cases. A dull pain in the chest was the first sign of illness in 13.4% and often persisted for a considerable time unaccompanied by any other symptom except some general malaise. Vague aches in limbs and trunk, with and without headache,ushered in the illness in 11.0%, and as these pains are so commonly found in natives as sequelae of Yaws, Syphilis, and other conditions the possibility of their indicating an early trypanosomiasis is important. Abdominal pain too is likely to be passed over as incidental in a native's life but it indicated a trypanosome infection in three cases. Dimness of vision was reported three times; in two cases there was no outward sign of occular defect,but in the third there was a severe keratitis which cleared up immediately with treatment following the diagnosis of trypanosomiasis.

(b) Duration and Course of Disease:-

Accurate estimation of the total duration of the disease from the onset of the first symptom till death was possible in 48 cases: 18 of these are included in this series, and are cases who were first seen practically moribund or at least too far advanced to be influenced by treatment; the remaining 30 were diagnosed by blood slides brought in from an outlying area, they died without treatment and their histories were carefully investigated at a later date. The average duration was found to be five months, the maximum ten and the minimum one month. This average duration appears to have remained constant throughout the epidemic, and a comparison of cases diagnosed in different years does not point to any increase or decrease in the virulence of the infection.

The course of the illness seen in the epidemic did not differ greatly in the average case from the recognised description to which reference has been made (p 2), and attention will only be drawn to particular points of interest.

The mode of onset has been detailed above because of the important bearing this has upon early diagnosis. The symptoms mentioned were the first signs of illness to appear but in the average case they did not remain alone as such, and combinations of headache, aches in the bones, thoracic pain, fever, etc., took place early in the clinical course.

These symptoms did not appear in any set chronological sequence ; each was seen alone or in conjunction with any other.

The history of early remission which is typical of African Sleeping Sickness was carefully investigated in every case. It was found that a daily remission,-i.e. an improvement in the mornings only, was practically constant, but a complete remission for a period of 1-3 weeks during which time the patient felt absolutely well only occurred in 25%. An amelioration of symptoms and a return to fair health was noted in another 26%, but there remained a large number in which no history of a real remission could be obtained.

There were three types of case in which the course of the disease differed radically from the classical description. One of these was that of acute onset with sharp fever and a rapid progression of symptoms, with high pyrexia and a fatal ending in from 1-3 months ; this was seen three times. The second was the extremely 'chronic' type with gradual onset, marked remission,and a very slow advance so that the patient was able to continue with his normal occupation for many months. Eight instances of this type were noted with histories of 8-12 months illness, and the following is one extreme example with a history of years :-

Case 267: /

Case 267: Diagnosed by peripheral blood infection. Middle aged man rather thin on admission but not wasted and still able to do light work. He had a history of three years' illness complaining of chronic chest pain and weakness. He had no physical signs in the lungs, responded immediately to treatment by 'Bayer' and is now fit and well. An attempt to diagnose the infecting trypanosome by animal inoculation was unsuccessful and he was termed an aberrant T. rhodesiense infection.

The third type, of which only two cases were seen, was characterised by an acute onset of illness with symptoms and Lumbar Puncture findings indicating grave pathological changes in the central nervous system but little systemic disturbance. The explanation of this type is not clear, but it seems as if the infection had been established for some time, and, owing to some pecularity in the strain of the infecting trypanosome, grave gradual involvement of the central nervous system had been going on while little or no evidence of toxaemia was apparent. The following is a brief summary of the cases referred to :-

Case 335. Known to be fit and working one day, he awoke during the night, fainted became semi-conscious and was brought in for treatment next morning in a stuporose, hypertonic and mentally irritable condition. Blood positive C.S.F. at high pressure, albumen greatly increased, cells 150 per cmm, no trypanosomes found.

Case 379. Young man well nourished had noticed nothing except a slight headahce five days before admission. On the sixth he collapsed suddenly on his way to work and was brought for treatment with paresis of lower limbs rendering him unable to stand. No headache or wasting. Blood negative on repeated examinations, Gland Puncture impossible, C.S.F.contained trypanosomes.

It is convenient here to refer to the type of case which has been called the 'Healthy Carrier'. By this is meant a person who has trypanosomes in his peripheral blood but absolutely no symptoms of the disease. The occurrence of this condition is naturally of vast importance in the epidemiology of the disease, but though cases have been described in T. rhodesiense infections the writer can find no evidence which proves that such are carriers in the true sense of the word, capable of undergoing spontaneous cure or remaining indefinitely with no symptoms of disease. In the course of many thousands of routine examinations of bloods made by the writer in the epidemic area in Ufipa only one case was found with a peripheral blood infection but entirely without symptoms; this was an infant of 11 months, obviously infected from his mother, who was carrying him on her back and was a definite case of Sleeping Sickness. The child was treated but relapsed shortly after.[1] Two other adult males diagnosed in routine examinations were practically without symptoms, but one admitted a history of slight headache and the other was excitable and had a marked tachycardia. The writer has , therefore, from purely clinical observations, formed the opinion that the so-called "Carrier" stage is merely a phase in the development of an infection of low virulence.

1. Case 375. Vide Appendix "A"

There is no doubt that in any single epidemic or endemic area a great variation in the course and general behaviour of cases occurs. Individual resistance may be a factor in producing this but does not afford a complete explanation, and it is more probable that a variation in the character and virulence of the infecting organism is mainly responsible. Proof of this statement may be available when further experimental work is undertaken which will compare strains obtained from actual cases representing the different clinical types.

(c) General Symptoms :-

A list of the principle symptoms together with the frequency of their occurrence in the series of 94 cases is tabulated below :-

Symptom	Cases	Symptom	Cases
Adenitis	86	Mental Dullness	11
Tachycardia	83	Bronchitis	10
Headache	79	Giddiness	6
Tremors	70	Splenic Pain	5
Wasting	68	Enlarged Liver	4
Leg Pains	59	Acute Mania	4
Oedema	54	Epileptiform Fits	4
Chest Pain	48	Conjunctivitis	4
Enlarged Spleen	33	Keratitis	3
Cardiac Abnormalities	32	Iritis	3
Arm Pains	28	Hyperaesthesia	3
Sharp Fever	27	Liver Pain	2
Abdominal Pain	23	Clonus	2
Cough	15	Paresis	2
Dimness of Vision	15	Vomiting	1
Diarrhoea	11	Itching	1

The above list represents symptoms found in all stages of the disease and conforms fairly closely to to findings previously reported in smaller series of Rhodesian Sleeping Sickness. When compared with any

similar compilation taken from a series of gambiense infections one essential difference becomes apparent; in the latter symptoms referred to the central nervous system predominate, while in the Rhodesian type the toxic manifestations are the more marked. This can be explained by the relative virulence of T. rhodesiense compared with that of T. gambiense: in the infections by the latter the chronicity of the disease allows time for grave pathogenic changes to take place in the central nervous system; in the Rhodesian type the extreme virulence of the infecting trypanosome produces rapid wasting and weakness, and though a leptomeningitis and cerebral infiltration will ensue, grave symptoms resulting from these changes will not necessarily be a prominent feature in an untreated case, as the sheer exhaustion of toxaemia with a failing heart will cause death.

Headache was a very common symptom in all stages of the disease, and was usually described as an acute throbbing pain localised in the temporal area. This may at times have been due to cerebral causes, but its early occurrence and the rapidity with which it yielded to treatment by 'Bayer' suggested that it was mainly a toxic phenomenon.

Pain in the chest was also very frequently noted, especially in the first two months of an untreated case. It was a dull pain referred to the sternum and did not appear to have any cardiac significance, nor was it accompanied by physical signs in the lungs. It might possibly be explained by the presence of a mediastinal adenitis.

Abdominal pain or discomfort was generally found early and was generally associated with constipation or diarrhoea. It yielded at once to specific treatment and is doubtless a true symptom.

Vague pains in limbs and trunk were found in cases with sharp fever and also in the more chronic cases. The limb pains were referred to the bones and joints and were not hyperaesthesias.

Enlargement of the spleen was found in 33 cases and in 3 there was accompanying pain and tenderness suggestive of acute engorgement or, perisplenitis. The enlargement extended to more than 4 inches from the costal margin in 4 cases, but gross enlargement was not usual. Concurrent causal conditions could never be excluded but the rapid reduction in size which followed purely specific treatment showed that trypanosomiasis was an important, if not the only, cause of the enlargement.

Occular disturbance entered into the histories of 15 cases. Of these the cause was traced to conjunctivitis in 4, to iritis in 3, to keratitis in 3, while in the remaining 5 there was no outward sign of occular defect but a definite history of dimness of vision.

Emaciation was extreme in all advanced cases. The rapidity with which it became apparent is characteristic of T. rhodesiense infections and there was some loss of weight apparent in every case after an illness of 1 - 3 weeks.

Anaemia was estimated by the blood haemoglobin percentage in every case as a routine, but the figures varied so much and appeared to be influenced by so many outside causes that they were considered to be unreliable. Extreme anaemia did occur in all late cases.

The erythema described as common in Sleeping Sickness was never seen on the dark skins of the natives dealt with. A dry scaly desquamation was observed in many instances, but no conclusion as to its significance was arrived at.

Other characteristics features of the disease met with in relation to the central nervous system, the cardiac system, the lymphatic system and in pyrexia will now be considered in detail.

(d) Central Nervous System:-

Many of the serious symptoms of Sleeping Sickness and most of the difficulties in treatment arise on account of the invasion of the central nervous system by the trypanosomes, so it is important to realise at what stage of the infection this invasion may occur. Certain observations made in the study of this series makes it possible to do this.

Some cases presenting a normal cerebro-spinal fluid after an illness lasting some months suggested that, as appears to be the case in T. gambiense infections, the invasion of the central system is a comparatively late event; but the recognition of such a condition as has been previously described by KEEVIL (1926), i.e. trypanosomes present in the spinal fluid with a cell count therein of only 3 cells per cmm, and the fact that many of the apparently normal fluids showed retrogressive changes later in spite of treatment which controlled the peripheral infection, cast some doubt upon the completeness of the escape of the central nervous system in those cases. Then, definite proof of early involvement was available in ten cases who were examined within three weeks or less of the onset of symptoms and showed abnormal spinal fluids, cells and albumen being increased in all and trypanosomes also present in 2.[1]

1. Cases, 368, 374, 376, 379, 380, 382, 383, 385, 393, 395. vide Appendix "A".

With this proof that the central nervous system commonly becomes involved at a very early stage, and considering that in some cases with abnormal spinal fluids there was no symptomatic evidence of the change, it becomes obvious that there are very few cases of T.rhodesiense infections, however early, in which the possibility of the central nervous system being involved can be excluded; and further, it follows that any arbitrary division of such cases into those with and those without central nervous system involvement is neither justified nor convenient.

Turning to the actual symptoms arising from the central nervous system it has been shown by such work as that of MOTT (1910) and WOLBACH and BINGER (1912) that the pathological change causing these is, broadly speaking, a meningo-encephalitis resulting from the local action of the trypanosomes. The symptoms themselves are important and can be classified as irritative, and (2) cerebral: the former including tremors, spasticity, epileptiform fits etc., and the latter the mental disorders arising from interference with the higher mental functions.

The occurrence of tremors in fingers and tongue at some stage of the infection was almost a constant finding. The coarse tremor commonly seen in a well established case was probably directly due to toxaemia and weakness but the fine, delicate tremor is of more importance. The incidence and persistence

of this sign was carefully noted in every case, and an examination of the clinical progress, lumbar puncture findings and final result of those in which it was found showed that it had a definite relationship to changes in the central nervous system; it was not seen in the early infection reacting well to treatment: its persistence after treatment meant that recovery was not complete; and its recurrence after a healthy spell was always suggestive of impending relapse.

A marked general spasticity, reflected in the gait and in the exaggeration of tendon reflexes was observed in 15%. Reflexes are, however, very difficult to elicit satisfactorily in natives and though marked exaggeration often accompanied changes in the nervous system the converse did not hold good; small variations from the normal were of no clinical value. Ankle clonus was noted in two cases; both of these had cell counts in the cerebro spinal fluid of more than 300 per cmm. and both proved fatal.

A condition of general hypertonus occurred in 6% and was invariably associated with degenerative changes in the cerebro-spinal fluid. This was a late symptom and with it was commonly found a stuporose but irritable mental condition; the patient being incapable of active movements, or too lethargic to perform them, and resenting all passive movements of head or limbs ; it appeared as if the general rigidity caused some degree of pain but a true 'Kernig' was not present. Though this condition had generally a

very grave significance it was found very early in one atypical case which has already been quoted.[1]

Evidence of advanced encephalitis was found in violent tremors and clonic contractions of limbs. It was noted in 9% , all far advanced, and all except 2% in relapse. These contractions and choreic movements occasionally become extreme but a true convulsion was not noted.

Epileptiform fits were recorded in 4%, all relapse cases. The history of these fits resembled that of the Jacksonian type but in one case there was an interesting history of recurrent attacks of 'Petit Mal' over a period of five weeks which terminated in a severe fit in which he lay unconscious on a fire for some minutes.

Symptoms indicating gross interference with the higher mental functions are not common in the T.rhodesiense form of Sleeping Sickness, and in an untreated case mental acuity is as a rule only dulled to an extent which can readily be accounted for by the bodily weakness. A stuporose delirium and mental confusion occurs late and is practically always a preterminal state.

Acute mania occurred in 4%, all relapse cases. In one case it was temporary and the patient recovered fair health, but the usual termination was progressive weakness and lapse into coma.

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1. Case 385. Quoted under Course of Disease p. 16

True paralysis did not occur in the series and the only case of paresis was No. 379 quoted above. Loss of control of the rectal and vesical sphincters was not noted as a paralysis as it only occurred as part of the general condition of coma preceding death. Aphasia too, recorded in three instances, was associated with stupor and was not a separate entity.

It was impossible to investigate sensory disturbances with accuracy but no gross abnormalities were noted. Hyperaesthesia as described by KERANDEL (1909) occurred in 3% only, and was never described voluntarily by a patient.

(e) Cardiac System :-

An opportunity of observing the clinical condition of the heart was afforded in 74 cases, and the abnormalities found are detailed in TABLE 2 and classified according to duration of diseases in individual cases when first seen. The figures when subdivided are small, but compared in percentages show the relative frequency of the various conditiond, and indicate the increase in frequency as the disease progresses.

Table 2 /

Table 2.

Cardiac Abnormalities :-

	Percentage Positive.			
Abnormality	Under 1 month	1-3 months	Over 3 months	Total
Irritability of Heart	72.4	92.3	91.3	83
Weak Heart Sounds	13.8	53.8	69.6	41
Bruits	6.9	15.	13.0	12
Dilatation	--	18.2	34.8	15
Alteration of Rhythm	3.5	21.0	22.2	14

Of the abnormalities found, irritability causing an instability of the pulse rate and a degree of tachycardia quite out of proportion to them pyrexia was by far the most common; it appeared in over 70% of the cases seen in the first month and later it becomes practically constant. In arriving at the figures quoted no pulse rate below 96 per minute with a normal temperature was recorded as abnormal but it is not the frequency of the pulse per se which is of importance so much as the variations which cannot be reasonably explained by factors such as excitement or alteration in temparature. A patient lying in bed may have a pulse beating steadily at 70-80 per minute but a slight exertion as sitting up or even the psychical stimuli provided by a routine examination to which he is

accustomed, will cause a jump to 120 or more. Pulse rates of 140-160 per minute were not rarities and were found when the heart appeared to be otherwise normal.

This irritability was a very early sign and in one case it was the unusually rapid and forcible beating of the carotids which prompted an examination and led to the demonstration of trypanosomes in the blood of an apparently healthy native.

Satisfactory treatment, that is treatment which results in the sterilisation of the blood and improvement in the general condition, was followed, in a very short time, by a steadying of the pulse rate; but in advanced and resistant cases, or in relapse, the condition persisted.

In two charts reproduced in Appendix B[1], the lack of relationship between pulse rate and temperature are well shown. The pulse rate was counted with the patient at rest and any element of excitement was eliminated as far as possible.

The other abnormalities recorded in Table 2 were distributed among 32 of the 74 cases. They represent, alone or in combinations all degrees of cardiac disorder from the simple loss of tone and subsequent weakening of the sounds at the apex, to complete disorganization of rhythm and heart failure, but the essential lesion which could explain all was a toxic myocarditis arising from the trypanosome infection. There is no proof that the trypanosome

1. Cases 267, 180.

toxin has any selective action on the myocardium ; general muscular wasting is inevitable and in that the myocardium is bound to be involved, but cases were noted with a marked degree of heart failure without a corresponding deterioration of the skeletal musculature and suggested a possible selective action.

As a result of myocarditis rapidity of the pulse would be expected and did occur, of course, in advanced cases where the heart was beginning to fail/for the purpose of prognosis this has to be distinguished from the irritability described above. The latter appeared at the very beginning of the infection when no other abnormality could be found in the heart and the pulse was not weakened, and it may have been entirely due to some intereference with the normal conductivity or innervation of the heart: it certainly did not adversely affect the prognosis in an early case.

In the absence of previous history it does not necessarily follow that the abnormalities noted at the original examination were not present before the disease was contracted, but the fact that they are really due to the infection seems to be established by their reaction to purely specific treatment: if the case was going to do well they disappeared almost immediately; if it proved resistant there was either only a temporary improvement or a progressive deterioration.

The condition of the heart at death appeared to depend upon whether the course of the disease had been acute and the patient was dying with little or no opportunity for treatment, or whether the case was one of relapse after prolongation of life by specific drugs. In the former the terminal feature was usually some grave alteration of ryhthm with a pulse rate of 160-200 per minute, and in the latter the usual coma was accompanied by a pulse rate of 45-70 per minute which only occasionally accelerated at the end.

(f) Adenitis :-

The typical adenitis due to trypanosome infections has often been described. It is a soft, discreet, enlargement; the glands are almost fluctuating in consistence, freely moveable under the skin, characteristically painless, and vary in size from that of a pea to that of a walnut.

Accurate observation and record of the adenitis present before treatment was possible in 87 cases in this series. In the average case the adenitis conformed to the above description, but painful glands were noted in eight instances and there was one case with an abscess in the axilla early in the course of the infection in which the possibility of suppuration in a trypanosome infected gland could not be excluded.

In a large percentage of the cases the enlargement was fairly uniform in the various groups and

was bilateral, but a few quite irregular distributions were met with. In one instance (case 334) the first symptoms of infection was the appearance of a unilateral chain of soft, tender, enlarged, glands running down the posterior border of the sterno-mastoid and obviously emanating from a painful, fluctuating swelling on the scalp ; there was one submaxillary gland enlarged on the same side, but no adenitis in any other of the superficial groups; the swelling and the adenitis subsided within two days of the exhibition of 'Bayer' and it was concluded that this was an example of inflammation arising in the direct lymph drainage from the site of an infecting bite, though it was the only case met with in the series where such a deduction was possible. As a rule the sequence of glandular enlargement cannot be worked out, but though the general adenitis arises so very early in the infection, it is bilateral, and involves the internal as well as the superficial groups, and it can be concluded with certainty that the blood infection plays a much greater part in its causation than any direct lymph drainage.

Table 3 :- /

Table 3:-

Incidence of Adenitis.

Stage of Disease	No. of Cases	Axillary Group			Cervical Group			Posterior Triangle			Submental			Epitrochlear.		
		T.*	H.	Neg.	T	H	N.	T	H	N.	T	H	N.	T	H	N
Developing	25	23	2	0	19	5	1	17	7	1	16	3	6	3	6	11
Progressive	50	48	1	1	29	12	9	26	16	8	28	10	12	25	14	11
Terminal or Late	12	2	9	1	3	7	2	0	10	2	1	6	1	0	9	3
Total	87	73	12	2	51	24	12	43	33	11	45	19	19	28	29	25
Percentage Posve		84%			59%			50%			51%			32%		

* T=Typical Gland. H=Palpable but hard. N= Not enlarged.

The results of the pretreatment examinations made are tabulated in Table 3 with the object of showing which groups were affected with the greatest relative frequency in the various stages of the disease. The cases were classified as early, progressive, and late; an early case was taken as one first seen in less than a month from the onset of symptoms, late cases were those in which there were great emaciation and weakness, and the progressive stage included all varieties between those two extremes. The areas considered are those usually investigated for diagnostic purposes; the inguinal group was excluded as being more likely than the others to be enlarged from other causes, but it must be remembered that, the absolutely typical swelling excluded, misleading figures are apt to be obtained in all areas owing to scalp infestations and infections, oral sepsis, etc.

The figures obtained in this series and quoted in Table 3 show that the axillary group was most constantly enlarged, and that the glands in the neck came next in importance. Again, they bring out the tendency to contraction and hardening of the glands as the disease progresses, until in the terminal stages, anything more than a hard and fibrotic enlargement was extremely uncommon.

The results of the routine examinations of glands made during and after treatment have not been recorded in Table 3 because it was found that

the swelling subsided and the glands became hard in the first few weeks of treatment, and no cases was noted where they subsequently regained the original character typical of the untreated infection. Even in relapse the glands remained hard, and in no instance did an exploratory puncture then reveal trypanosomes in the juice.

The diagnostic value of adenitis and gland puncture has been referred to in the section on 'Diagnosis'.

(g) Oedema :-

Oedema was a very common symptom and was noted in 57% of the complete series. All degrees were met with, from a slight bogginess elicited on pressure on the dorsum of the feet, to an extreme swelling of feet and legs. A puffy swelling on the forehead appeared to be characteristic in certain groups of cases, and in others, where little or no swelling was apparent on the legs, an oedema was easily demonstrated over the spines of the lower vertebrae.

The time of onset varied in different cases: it was the first symptom recorded in two instances, in about 5% it developed after the second month, but in the average case it was apparent by the 2nd-6th week of illness. Occasionally there was a history of spontaneous disappearance, and at times it was of a temporary nature due to long walks, but as a reult it came on gradually and

persisted till treatment was started or until emaciation and dehydration became extreme in the terminal stage.

It appeared to be due mainly, if not entirely, to the action of the trypanosome toxins - presumably on the endothelium of the blood vessels and capilliaries - and certainly had no constant relation to helminthic infection, anaemia, or to cardiac and renal conditions. Almost invariably it cleared up within a week of the first exhibition of 'Bayer', and it did not recur during treatment or in relapse although the other possible causal factors indicated remained unchanged. Case 344 was an extreme, though by no means an isolated, example of this: the stools in that instance were full of ankylostome ova, the blood haemoglobin was 20%, the heart sounds were weak and there was a mitral systolic murmur; and still the marked swellings on feet and legs cleared up completely in 7 days after the first gram of 'Bayer'.

The absence of gross swellings in relapse cases with a peripheral blood infection can be explained by allowing that the relapse strain of trypanosomes has a much lowered toxicity.[1]

BATTAGLIA (1927) made interesting observations on histological changes which he found in the thyroid and parathyroid glands in trypanosomiasis, and he concluded that the oedema - which he described as myxoedematous - was due to these changes,

1. Authority for this statement under 'Relapse p. 47

If that were so, however, it would be difficult to account for the spontaneous disappearance of oedema which occasionally occurs, and for the rapidity with which it clears up after the exhibition of 'Baver.'

Oedema is of interest because of its diagnostic value in a mass campaign. It is a sign readily noted by the natives themselves who have their own distinction between it and the swellings of ankylostomiasis. The latter - 'Safura' as it is called locally - is described by them as being a general puffiness of the whole body, whereas in 'Malali', os Sleeping Sickness, the swellings are said to be localised and the accompanying degree of wasting obvious.

(h) Pyrexia :-

Records of the temperature are available in 78 cases, and though these are necessarily incomplete, and do not give an entire history of every case, they represent every stage of the disease and when summarized show the principle features of a complete course.

At the onset there was, in practically every case, a febrile disturbance of some sort, though this might not be noted by the patient. In those cases with a slow, insidious, onset it might only be an occasional evening rise to perhaps 100°F., with complete remissions of a day or two between subsequent isolated rises; but in the acute type

there was a sharp initial fever with a maximum of 103-104°F. occasionally sustained with incomplete morning remissions for as long as a fortnight before it settled down to the definitely intermittent pyrexia of the established infection.

In this established stage the periods of remission were often as long as a fortnight so that unless a record was kept for a considerable time the disease at this stage appeared to be afebrile. This character was maintained throughout the course, but towards the end in an untreated case, it was usual to find the temperature settling down at a subnormal level, to rise, perhaps, a few degrees as death occurred. There were cases where the temperature never really assumed the intermittent form but remained an irregular, hectic fever. These were rare and indicated a very virulent infection which ran a rapid course.

After treatment has been instituted it was usual for the temperature to settle down and to remain within normal limits for the remainder of the treatment course; if a complete cure had been effected it of course remained normal, but even when subsequent events proved that the disease had not been eradicated, a temporary success was accompanied by an absence of pyrexia until the relapse or late complication occurred. Small rises of temperature - apart from those due to drugs - were not uncommon during the early treatment, and where the administration of drugs was continuous

these did not affect the prognosis adversely. On the other hand if the temperature did not settle down within three weeks it was considered abnormal, and indicated that some complicating factor was present or that the infection was going to prove intractable to the drugs employed. Unexplained rises of temperature coming after an apparently healthy period must be taken to mean that there are trypanosomes still active and that a relapse will follow.

In relapse the pyrexia behaved very much as in the untreated case and there were all variations of severity from the occasional evening flickers to the irregular remittent type which could only be imperfectly controlled by drugs.

Apart from the steadying of the temperature which followed the successful administration of specific drugs there was with some a febrile reaction directly attributable to the drug. 'Bayer' was the most important in this respect and records were kept of 56 cases in this series where it was given alone at the start of treatment. The results of these observations are summarised in Table 4. The dosage of the drug was as follows :- 1st and 2nd doses of 1 gram each given intravenously at 48 hours' interval with a 3rd dose of 1 or 2 grams given 48 hours after the second; later doses were at irregular intervals but in no case was more than 2 grams given as a single dose. The febrile reaction

usually commenced in 4-6 hours after the injection, the temperature was at its maximum in 10-12 hours, and it fell to normal again in 24 hours. The reaction following 2nd or 3rd doses was less severe than the original except in two cases where there was a negligible rise after the 1st dose but a sharp reaction after the second. The table does not include cases where 'Bayer' was given in relapse. In such cases there was often a slight febrile reaction but it was never so great as that occurring when the drug was given at the start of treatment.

There is interest in these figures from the point of view of prognosis, and a careful comparison of the reactions with the final result of treatment has shown that the best clinical result can be expected in cases where there was a sharp rise of temperature after the first dose, and a slight one or none at all on subsequent occasions. Absence of fever was not satisfactory and appeared to indicate a very weak response to the drug, and inability on the part of the tissues to combat the infection. Extracts from the actual charts of a few cases are included in Appendix "B" to illustrate some of the points in pyrexia referred to.

Table 4 :-

Febrile Reaction following 'Bayer 205'.

Dose	No of Cases	No Reaction	98-100°F	100.1-102°F	over 102°F
1st	56	25%	25%	35%	15%
2nd	56	60%	31%	8%	nil
3rd	42	80%	11%	8%	nil
Late Doses	22	95%	5%	Nil	nil

V. COMPLICATIONS.

The most serious complications of Sleeping Sickness are acute pulmonary and abdominal diseases, and the various parasitic infections prevalent among native races in the tropics.

In this series pulmonary conditions were much less common than might have been expected; they included acute bronchitis present in 5%, and one case of broncho-pneumonia.

Acute diarrhoea occurred in 12%. In five cases it developed early and yielded at once to treatment by 'Bayer', but in the others its incidence was late in the course of the illness and then it was a grave complication, causing rapid prostration and being very intractable to treatment. This condition is included here among the complications,but there is evidence to show that it might more properly be described as a symptom and be termed a direct result of the activities of the trypanosomes. BALFOUR (1906) has described congestion and ulceration of the gastric and intestinal mucosa in experimental infections in animals : KERANDEL (1909) notes its early occurrence : THIREAU (1909) concluded on pathological grounds that it was due to the localisation of trypanosomes in the mucosa of the intestine:Mott (1910) reported inflammation of the Peyer's patches as part of the general invasion of the lymphatic structures. The

writer had the opportunity of performing a post-mortem examination on two cases with acute diarrhoea as a terminal symptom but no very characteristic picture was presented by the macroscopic appearance of the intestine; small irregular areas of congestion and infiltration were seen, the whole bowel was thin and transparent, mesenteric glands were enlarged and fibrotic, and there was no gross ulceration or necrosis. The occurrence of abdominal pain has been briefly referred to in the symptomatology (p. 19) ; this is clinical evidence of a localised action of the trypanosomes in the abdomen, but it can be accounted for by the adenitis which occurs in the abdominal groups of glands.

Pathogenic helminths occurred in the series as follows : Ankylostomes 71%; Schistosoma mansoni 3%; S.haematobium 1% Ascaris 2%; Oxyuris 3%.

In view of the extremely common concurrent Ankylostome infection in trypanosomiasis, an attempt was made to estimate the bearing this had on the clinical course of the disease and to investigate the suggestion made by DUKE (1923) that ankylostomiasis might be an epidemiological factor rendering a population particularly susceptible to trypanosome infections.

In the area under consideration a simple microspic examination of the stools of 250 unselected natives gave an ankylostome infection rate of 72%;

and in 60 Sleeping Sickness cases examined by the same technique the percentage positive was 71. Accurate estimations of the numbers of ova and worms was not made, but rough notes of the severity of the infection were kept and the percentages of light, moderate, and heavy infections proved to be almost identical in the two groups. Further, in order to observe the effect of the ankylostomes on an established trypanosomiasis, all cases with light or moderate infections were left without anti-helminthic treatment, and it was found that these reacted to the trypanocidal drugs as well as the negative cases, although subsequent examinations showed the numbers of ova in the stools to be unchanged. On the other hand, the reaction to specific treatment in six cases of heavy infections was very unsatisfactory until the helminths were got rid of.

As a result of these observations it was concluded that (1) a true ankylostomiasis militates against recovery from Sleeping Sickness but the mere presence of worms has little or no effect ; and (2) the fact that the infection rate was lower in Sleeping Sickness cases than in the normal population does not bear out the hypothesis than an ankylostome infection predisposes to trypanosomiasis.

Malarial parasites were frequently discovered during the routine examinations of Sleeping Sickness bloods, but as a rule they produced very few

symptoms. At times headaches and pyrexia arising therefrom were liable to misinterpretation, but the condition yielded rapidly to treatment when the diagnosis was made.

Syphilis and Yaws also had to be reckoned with as complications, and the possibility of an abnormal cerebro-spinal fluid being due to this cause remembered.

(VI. RELAPSE.

In Rhodesian Sleeping Sickness relapse should be described as being of two types, microscopical and clinical: the former meaning the reappearance of trypanosomes in the blood, gland-juice, or cerebro-spinal fluid, after a period during which their presence could not be demonstrated; and the latter the recurrence of clinical signs and symptoms after treatment in a patient who has recovered apparently normal health, or at least progressed favourably towards that condition. It is possible that inoculation experiments, or a more exhaustive search using a concentrating technique, might result in the demonstration of the parasites in the latter type, but its recognition as a clinical entity is necessary.

After the combined 'Bayer' and Tryparsamide treatment given in this series a relapse as defined above occurred in 19 cases. Of these relapses, 10 were diagnosed on clinical grounds alone, and 9 were diagnosed microscopically, 2 with the blood alone positive, 2 with blood and cerebro-spinal fluid positive, and 5 by the presence of trypanosomes in cerebro-spinal fluid only. These figures show that it is often impossible to demonstrate the parasite in a definite relapse, and they show the relative rarity of the recurrence of a heavy infection in the peripheral blood.

Practically every one of the above cases had received more than 25 grams of Tryparsamide following 'Bayer', and in two cases repeated microscopical relapses took place after 49 grams of Tryparsamide.

The interval between cessation of treatment and the diagnosis of relapse varied from a minimum of three months to a maximum of eighteen, the average being 7 months.

The symptoms and signs which occurred in relapse differed somewhat from those found in an untreated infection. Oedema and adenitis, for example, were seldom present; a patchy oedema was found but it never amounted to extreme swelling, and though small palpable glands might be evident these were really the hard fibrosed relics of the original adenitis and were not indicative of a fresh inflammation. Headache of varying degree of intensity

was the constant phenomenon and this, accompanied by fine tremor of the fingers and irregular rises of temperature, was all the evidence required for the resumption of treatment. Confirmation was on occasion obtained by the demonstration of parasites in blood or cerebro-spinal fluid; and even if negative for trypanosomes, an examination of the latter usually displayed retrogressive changes in cell count and albumen content.

If a relapse did not receive treatment the subsequent course was rapid; weakness became apparent and progressive, and prostration ensued in a month or less, the result of treatment, too, was seldom satisfactory; Apparent cures were obtained but were not often permanent, and with each recurring relapse treatment became less and less efficacious.

It is in the later stages of a relapsed case that the extreme manifestations of central nervous system involvement become apparent; the mentality is dulled, giddiness, fainting and epileptiform fits occur, and a stuporose delirium, mental confusion, or even acute mania may follow and persist till the final unconsciousness of weakness and coma.

There seems to be little doubt that in relapse,- i.e., in a partially or unsuccessfully treated case - a new strain of trypanosomes has been created which is not only more resistant to treatment, but has a much lowered virulence. This has been suggested by experimental work on animals reported by

LUPOLD (1924) TALIAFERRO (1926) and THOMSON and ROBERTSON (1926) and is confirmed by clinical observations on human cases. The writer has, for example, four cases where routine examinations showed the presence of trypanosomes in the blood or cerebro-spinal fluid after treatment although the patient professed perfect health and had no symptoms; from comparison with other similar instances the ultimate fate of these is certain, but still the strain had most certainly decreased in virulence and become practically drug-fast; before the original treatment the parasites had reduced the patient to an extreme degree of weakness in a very short time, whereas the relapse strain existed in the vital fluids producing no acute symptoms.

This gives an explanation of the preponderance of mental symptoms in relapse cases. In an untreated case the unhampered activities of the highly virulent trypanosomes produce a toxaemia which causes death more by the action on the heart and other viscera than by its interference with the vital functions of the brain; when treatment is given toxaemia disappears and there is progress towards clinical recovery; but the central-nervous infection is not completed controlled, and the prolongation of life now affords an opportunity for the continuance of the chronic inflammatory process in brain and cord, maintained by the relapse strain of trypanosomes, which goes on until the border-line of disturbance compatable with apparent health is passed and a re-

relapse occurs, the degree of meningitis and encephalitis now being much greater than could develop in an untreated infection.

VII. TREATMENT.

(a) Selection of Treatment :-

The treatment employed almost exclusively in this series was a combination of the two drugs' 'Bayer 205' and Tryparsamide; a short preliminary course of the former being followed by a more intensive dosage of the arsenical drug.

The selection of this method was based upon a consideration of the early experimental work done on 'Bayer' by YORKE(1921), KLEINE and FISCHER (1922, 1923, 1924), FONTANA (1924), VAN DEN BRANDEN and VAN DEN HOOF (1923, 1924), LOW and MANSON-BAHR (1922), CHESTERMAN (1924) and others; and on Tryparsamide by PEARCE (1921), PEARCE and BROWN (1924), CHESTERMAN (1923, 1924) and others. This work shows, in short, that though 'Bayer' has a powerful and immediate trypanocidal action on the peripheral blood, and produces what often appears to be dramatic cures, its action is by no means always permanent, and, moreover, its low power of penetration renders it ineffective against infections of the central nervous system. Tryparsamide on the other hand, has a great power of penetration; and, though its

parasiticidal action is relatively slow and weak, its penetrability, combined with a certain tonic effect upon the tissues, makes it singularly useful in dealing with deep seated infections.

It appeared, then, that a course of these two drugs given in sequence would be successful in combining the advantages of both, but it was realised that the dangers of both would also be present and possibly exaggerated.

(b) 'Bayer 205' :-

(1) Composition and Mode of Action:-

'Bayer 205' was introduced by the Bayer Company in 1919, but at that time little was disclosed regarding its composition save the statement that it contained no therapeutically active metals or metalloids. Its molecular constitution was published by the MEDICAL RESEARCH COUNCIL (1921), a supposedly identical substance was prepared by FOURNEAU TREFOUEL and VALLEE (1924), and it is now believed to belong to the branch of urea-substitution products of the aromatic group.

The mode of action of 'Bayer' in the body was for a long time in doubt, but the question has been to a great extent settled by such work as that of FREUND (1925), KLEIGER and WEITZMAN (1925) and ROEHL (1926), and it is now generally agreed that that the action of the drug is not due to any new substance formed in the body but is a direct trypanocidal one. Opinion is divided as to the length

of the time the drug remains active in the body, but even if it is stored in the tissues a certain concentration must be maintained, and repeated doses are therefore necessary in therapeutics and prophylaxis.

(2) Clinical Reactions :-

In the treatment of this series more than 250 separate doses of 'Bayer' were given without accident of any kind. The method of administration was intravenous injection whenever possible, one gram of the drug being dissolved in 6-8 cc. of sterile water. In a few instances where intramuscular injection was necessary, there was slight pain but no abscess resulted and that route appeared to be quite efficacious.

Evidence of renal disturbance occurred in 27% of the cases treated. This normally amounted to a simple albuminuria appearing in from 1-10 days after doses of 1-2 grams, and though in three cases there were casts, blood-cells, and signs of a pretty sharp renal affection, present in the urine it was never necessary to interrupt treatment on that account, and the condition rapidly cleared up.

The febrile reaction after 'Bayer' has been noted under 'Pyrexia' (page 38). After the first dose 10% of cases complained of a feeling of burning over the body, followed by shivering, and at times there was an increase of an existing headache; in one case there was a definite rigor six hours after

after administration and a sudden rise of temperature to 104.6°F., but this subsided within 24 hours. Marked reaction is rare, however, and normally the beneficial action of the drug is exerted without any preliminary discomfort to the patient.

(3) Sterilization of the Peripheral Blood :-

A short series of 12 cases were carefully observed in order to ascertain the time in which the peripheral blood became negative after the administration of 'Bayer'. The cases when diagnosed had a peripheral blood infection and had received no previous treatment. The dosage of 'Bayer' was 1 gram on the 1st day, 1 gram after 48 hours, and 2 grams on the 5th day; the blood was examined (two thick drop preparations stained by 'Giemsa') hourly after injection for 18 hours, again at 24, 36 and 48 hours, and then daily for a week after the second dose had been given.

The average time by which sterilization was complete was 9½ hours, the maximum being 15 and the minimum 6 hours. In all the cases observed no recurrence of trypanosomes was found during the period of observation with the exception of the following case :-

> Case 344:- Young woman, ill 3 months. Blood became negative in 8 hours, remained negative till 48 hours when one trypanosome was found in the two slides. The blood became negative after the 2nd gram of 'Bayer" and remained so.

The persistence of trypanosomes in the gland

juice after treatment was investigated in 25 cases, gland puncture being done 24 hours after the first gram of 'Bayer.' In 23 of these the result was negative and in the remaining two the tyrpanosomes disappeared after the 2nd gram of 'Bayer'.

A mass of routine examinations of the blood performed during and after the combined 'Bayer' and Tryparsamide course has convinced the writer that once the blood has been rendered free from trypanosomes it remains so during the course: relapses which subsequently occur have been consider above (page 44). When the course is interrupted, however, it does not follow that the sterilization will be complete, and an opportunity of observing this was afforded in two instances. The two cases quoted below were diagnosed by blood slides; they received 'Bayer', but no Tryparsamide was available and they were first seen by the writer on his return to the treatment centre :-

Case 314. Young man, ill 8 months. Received 4 grams of 'Bayer.' Examined 7 days after last dose peripheral blood was negative. but axillary gland puncture strongly positive.

Case 318. Young man, ill 6 weeks. Received 2 grams 'Bayer' on alternate days. Examined 12 days after last dose the peripheral blood was found to be strongly positive for trypanosomes.

The chart of Case 318 is reproduced in Appendix 'B'; it shows a slight rise of temperature on the 11th day after 'Bayer' which possibly was coincident

with the return of trypanosomes to the peripheral blood. Observations on this subject are incomplete, but the writer has often noted similar rises in from 6-12 days after 'Bayer', and it is possible that these indicate a recovery phase in the trypanosome infection. This, and the other observations recorded above, showing that the action of 'Bayer' is not always complete, appear to the writer to form an argument in favour of leaving as short intervals as possible between the early doses in any course of treatment.

To sum up, the place of 'Bayer' in a course of treatment is undoubtedly at the outset when its powerful trypanocidal action which will pave the way for the more penetrating arsenical ; there is too the advantage of the immediate amelioration of symptoms which follow in all except the very advanced cases within a short time of the first and second injections. Three or four grams of 'Bayer', given in 1-2 gram doses on alternate days, will produce a feeling of well-being which amounts to practically normal health in an early case; while even if the disease is moderately far advanced the continuance of pain or gross discomfort is uncommon. In relapse, clinical or microscopical, 'Bayer' is also useful ; it has apparently no action on trypanosomes in the cerebro-spinal fluid, but it will temporarily reabolish a blood infection and control headahce much more speedily than will Tryparsamide.

The latter drug is essential in such cases, but 'Bayer' is very useful clinically.

(c) Tryparsamide :-

Since the pioneer work of Miss Pearce in 1920 much has been done with Tryparsamide in the treatment of T.gambiense infections, and its value in that variety of the disease has been proved, but there is comparatively little date as to its effect on the rhodesiense variety. Recent work in Tanganyika Territory by MACLEAN (1927), DYE (1926), and KEEVIL (1926) has proved that in Rhodesian Sleeping Sickness Tryparsamide alone is inferior to 'Bayer', both in the immediate sterilization of the blood, and in the maintainance of it in that condition; and it was commonly found that the persistence or recurrence of a peripheral infection after as much as 25 grams necessitated the administration of Bayer before satisfactory results could be obtained. This does not happen when the Tryparsamide is given immediately after a short course of Bayer, and in the course of constant routine examinations in this series there was not a single instance of the blood becoming positive during continuous treatment.

The great danger of Tryparsamide is generally recognised to be its apparently selective action on the optic nerve, the tendency to cause a neuritis, or even an atrophy which may go on to total blindness, and the problem in the Tryparsamide treatment

of Sleeping Sickness is how to administer a sufficient dosage of the drug in such a way that it will have the maximum effect on the parasites with the minimum risk of causing damage to the optic nerve. There is, unfortunately, no fixed saturation point at which the nerve becomes affected; there are individual variations in parallel cases, and a predisposition to the affection in cases with a severe involvement of the central nervous system or previous occular trouble. Wide spacing of the Tryparsamide doses is not always a safeguard, as the causal dose in some cases has been given as long as three weeks after the previous one; and again if very small doses are given over long periods there is a danger of producing a drug-fast strain of trypanosomes. CHESTERMAN (1924) was of the opinion that the sensitiveness of the optic nerve could be avoided if intensive doses of the drug were given over a short period, and that has been largely borne out by observation in the treatment of this series. Chesterman was referring to T.gambiense infections, however, and an amount of Tryparsamide which seems to control that type will not be effective against T.rhodesiense.

During the treatment of 77 cases who received full courses of Tryparsamide a degree of optic atrophy developed in 19. This went on to total blindness in 2 patients, both of whom received 29 grams in 4 weeks; a very severe dimness of vision persisted in 1 who received 17 grams in 19 days; 3 had a slight

but permanent blurring of distant vision; but in the remaining 14 the disturbance was purely temporary and disappeared in from 2-3 weeks. These accidents occurred mainly when the injections had to be left in the hands of the native staff, and there is no doubt that the incidence could be greatly reduced if facilities for examination and detection of early changes were always available.

When Tryparsamide is given in conjunction with 'Bayer' its independent action cannot be accurately estimated, and the results of treatment must be considered in the light of the combined action of the two drugs. It is apparent, however, that the place of Tryparsamide is in the following up of an initial treatment by 'Bayer.' Tryparsamide maintains a sterilization of the peripheral blood which it cannot itself create with any certainty, and, in a number of cases at least, it reaches the deeper tissues and establishes the position there.

(d) Routine Treatment and Final Results :-

As has been already indicated the routine treatment in this series was a combination of 'Bayer' and Tryparsamide. Whenever the diagnosis was established treatment commenced with the course of 'Bayer' which usually amounted to 2-5 grams given in 1-2 gram doses on alternate days. The first dose for adults was always 1 gram, and the maximum given in one dose was 2 grams. The course of Tryparsamide followed in from 4-10 days after the last dose of

'Bayer' : the actual dosage was varied throughout the series, partly intentionally and partly owing to the occasional shortage of drugs and difficulties in supervising treatment. In the earlier cases it was intended to give four weekly doses of 2, 3, 4, and 4, grams followed, after 14 days' interval, by four more weekly doses of 3, 4, 4, and 4, grams, and in the later cases a more intensive dosage commencing with 2, 3, 4, 4, and 4 grams at intervals of 5 days, with a subsequent course of four more doses at weekly intervals. In 1927 a trial was made of a short, intensive course of 5 grams of 'Bayer' and 15 grams of Tryparsamide all given within 25 days: there has not yet been a sufficiently long period of observation of these cases to allow any positive inference to be drawn, but it seems as if further treatment will be necessary as two cases relapsed microscopically within a few months of the cessation of treatment.

Details of treatment and the final results in all cases are given in Appendix "A". In Table 4 the end results of 63 cases who have been observed for one year or more are summarized; cases dying while under observation being included.

Table IV. /

Table IV.

End Results of Treatment. (Cases observed for one year or longer.)

Duration of Symptoms	Total No. of Cases.	Recovered and remain fit	Relapses and Imperfect Cures	Died.
Under one month	24	66.7%	16.7%	16.6%
1 to 3 months	16	25%	31.3%	43.7%
Over 3 months	23	26.1%	26.1%	47.8%
Totals	63	34.9%	23.8%	41.3%

The figures given above include all cases, even those who were moribund when treatment started, so that the numbers for 'apparent cures' are really understatements, and the use of the two drugs in combination appears to be a reasonably successful method of treatment. Cases showed a highly individualistic reaction to treatment and the end results of seemingly similar cases varied greatly; but the general conclusion arrived at as a result of a detailed study of the series was that if the Bayer and at least 25 grams of Tryparsamide were given within 2 months of diagnosis the size and the spacing of the doses was not of paramount importance. The vital factor, and this is strongly brought out by the figures in the Table, was the stage of the disease when treatment is started, but

but failures in early and promising cases remind us that in the virulent rhodesiense infection there is an invasion of the deeper tissues within a very short time of the occurrence of the premonitory symptoms which an intensive dosage of the most powerful drugs we have at our command cannot always eradicate.

An analysis of the series with a view to ascertaining the effect of treatment - mainly Tryparsamide presumably - on the central nervous system shows thatm though a marked clinical improvement together with a fall in the cell count of the cerebro-spinal fluid has taken place in many instances of severe involvement, it is rare for even a heavy and prolonged dosage to control a far advanced case, and there are even instances where the spinal fluid has deteriorated despite treatment in a comparatively recent infection.

(e) Fourneau:-

Fourneau was used in four cases. Its general action seemed to be very much the same as that of 'Bayer', but there was not sufficient data for any conclusion to be drawn as to its true value.

VIII. CONCLUSIONS.

(1) The object of the paper is to record some clinical observations made during the study of 94 consecutive cases of Rhodesian Sleeping Sickness.

(2) The main factor in the epidemic spread was man-fly-man transmission. The occurrence of human cases with no history of contact and the high T.*brucei* infection rate among the local fauna are recorded, as the possibility of there being some reservoir cannot be excluded.

(3) The incubation period is probably between 1-3 weeks.

(4) The average duration of the illness is five months.

(5) There was an acute febrile onset in 24% of cases. Variations in the subsequent course are found and it is considered that these are due to the existence of strains of trypanosomes of different virulence.

(6) The central nervous system may be involved at a very early stage. This results in grave pathological changes, but the virulence of the infection is such that symptoms arising from its effect on the heart and other viscera predominate over those due to central nervous system involvement until the last few weeks of the illness. Cardiac symptoms are important and the essential lesion is a toxic myocarditis.

(7) The axillary group of glands are those most constantly enlarged.

(8) It is in cases which have relapsed after treatment that mental symptoms are most pronounced. In relapse a new strain of trypanosomes has been created, of lowered virulence but resistant to the action of drugs.

(9) 'Bayer 205' has a strong and immediate effect on infections of the peripheral blood but its action is not always permanent and it cannot penetrate into the deeper tissues. Trypar-samide is slower in action but it maintains a sterilization made by 'Bayer' and it can exert a beneficial action on the central nervous system.

(11) Treatment by 'Bayer' should be followed immediately by Tryparasmide. A routine treatment by this method gives satisfactory results if treatment is started early in the course of the illness, but even the most intensive and prolonged doses of the two drugs in combination cannot be relied upon to effect a cure if the disease is well established.

APPENDICES.

A. General Summary of Cases.

B. Extracts from Charts.

C. Trypanosomes found in Game.

APPENDIX "A"

GENERAL SUMMARY OF CASES ARRANGED IN CHRONOLOGICAL, ORDER.

Abbreviations:- M = Male; F = Female; B = "Bayer 205"; T = Tryparsamide; Fo = "Fourneau"; CSF = Cerebro-Spinal fluid; C = Cells; Ts = Trypanosomes; D = at diagnosis.

Case No.	Sex	Age	Estimated Duration of Symptoms	Condition when Diagnosed	Initial Treatment = in gms	Duration of T. Course	Relapse Treatmeant	Cerebro-Spinal Fluid: Time elapsed from Diagnosis	Cerebro-Spinal Fluid: Result of Examination	Total period of Observation	Reaction to Treatment and Final Result.
33	M	10	3 mths	Thin & weak just able to walk	B. 2.1		B2 T 24	3 yrs	C60: Ts-	3 yrs	Apparent cure after 'Bayer' relapsed in 12 mths. Since then temporary recoveries and relapses., - last seen comatose
148	F	45	3 mths	Wasted & weak; just to walk slowly	B 2 T 27	9 wks		20 mths	C 0: Ts-	30 mths	Reacted well to treatment : remains well; apparent cure.
152	M	20	5 mths	Emaciated: unable to walk	B 2 T 31	10 wks		28 mths	C 10 Ts-	30 mths	Reacted well to treatment ; remains well; apparent cure.
159	M	45	8 mths	Emaciated; just able to walk	B 1 T 27	8 wks		16 mths 20 mths	C 390 Ts- C 280 Ts-	30 mths	Good recovery;remains fit; no relapse but rather weak.
161	F	25	1 mth	Emaciated; able to walk	B 1 T 16	7 wks				30 mths	Good recovery; remains fit.
180	M	20	5 mths	Thin & weak able to walk	B 2 T 26	11 wks				7 mths	Partial recovery; remained nervous & weak. Died.
182	F	30	2 mths	Condition fair; no wasting	B 2 T 26	10 wks	B2 T 40	13 mths 17 mths 19 mths	C 100 Ts- C 400 Ts++ C 480 Ts++	22 mths	Good recovery;relapsed 8 mths; recovered; 2nd relapse 13 ", recovered,3rd relapse 21 ", became epileptic: Died.

183	F	10	1 mth	weak,thin able to walk	B 1 T 12	9 wks				8 mths	Improved but nervous & weak; complete relapse at 8 mths; fainting fits: delirium: Died.
184	M	25	1 mth	weak,thin,able to walk	B 2 T 27	9 wks	T2			11 mths	Recovered fair health; relapsed at 8 mths;prostration, low delirium;Died
188	M	20	2 mths	Shaky,walking about,no wasting	B 2 T 27	9 wks	B 1 :	D	C170 Ts+	25 mths	Recovered good health; gradual relapse at 18 mths- blood +ve 24: condition poor,able to walk, receiving more treatment.
192	M	30	7 dys	Feverish,otherwise fit.	B 2 T 19	3 mths				24 mths	Recovered normal health, remains well.
193	M	25	2 wks	Thin, weak,walks short distances	B 2 T 27	3 mths	B 3 T 14	15 mths	C270 Ts+	24 mths	Recovered good health, relapsed 15 mths, Blood +, recovered, remains fit and working.
194	M	25	---	Detected in routine examin.	B 2 T 19	3 mths				24 mths	Excellent result,remains fit.
197	F	30	2 mths	Wasted,weak, unable to walk alone	B 2 T 11	3 mths				12 mths	Never regained strength; became maniacal - Died.
198	M	25	2 Dys	Feverish,otherwise fit	B 2 T 23	3 mths				24 mths	Good recovery ; remains fit.
199	M	30	1 mth	Wasted,unable to walk	B 2 T 20	2 mths				24 mths	Recovered slowly; now fit & working.
200	M	45	3 mths	Weak,wasted walks slowly	B 1 T 28	5 mths				24 mths	Excellent recovery;now fit & working.
202	M	30	4½ "	No wasting, walks well, weak	Fo 17			1 mth	C40 Ts-	2 mths	Progressed favourably for 1 mth, then gradual decline to coma. Died.
203	M	13	2 mths	Thin,just able to walk	Fo 16					5 wks	No real recovery. Died.
216	M	50	4 mths	Wasted,cannot stand alone	Fo 14					2 mths	No improvement ; Died.
218	M	40	3 mths	Wasted, just able to stand	B 3						No improvement - Died
219	M	65	2 Mths	Weak,emaciated old man just able to stand.	B 3 T 33	9 wks	T 12	1 wk 12 mth	C 60 Ts- C 40 Ts-	22 mths	Recovered slowly - given 2nd T course remains fit though weak
248	F	30	2 /								

248	F	30	2 Mths	wasted, able to walk	B 2 T 29	7 wks				9 mths	Apparently progressing well - went off on a journey - reported Died.
256	M	40	5 Mths	Emaciated, lethargic, can walk & help.	B 2 T 29	4 wks		11 mths 16 mths	C 140 Ts- C 250 Ts-	21 mths	Slow recovery - remains shaky, but fit for light work.
257	F	20	5 Mths	Emaciated, dull, cannot stand alone	B 2 T 33	13 mths		7 mths	C 400 Ts-	13 mths	Became stronger, fair health, relapsed at 12 mths. Died.
258	M	35	1 Mth	General weakness, no wasting	B 2 T 29	5 wks		17 mths	C 310 Ts-	21 mths	Recovered slowly, now remains fit, but totally blind.
259	M	40	3 Wks	Fit. c/o headache only	B 2 T 29	4 wks		11 mths	C 0 Ts-	18 mths	Excellent Recovery.
260	M	35	5 Dys	Fit c/o headache & fever	B 2 T 30	4 wks		11 mths	C 48 Ts-	18 mths	Excellent Recovery.
267	M	40	?	c/o chronic weakness c chest pain 3 years	B 2 T 34	8 wks		10 mths	C 2 Ts-	20 mths	Reacted immediately, remains in normal health.
268	M	30	2 Mths	Emaciated, just able to walk	B 2 T 34	9 wks		3 mths	C 380 Ts+	17 mths	Slight improvement, gradual decline - Died
269	F	35	3 wks	Thin, anaemic, walks well	B 2 T 23	10 wks				7 mths	Improved; untraced reported Died.
271	M	25	3 wks	Good condition c/o headache & weakness	B 2 T 30	9 wks	T 5	D 10 mths 17 mths	C 100 Ts - C 180 Ts- C 540 Ts-	20 mths	Improved rapidly to good health; relapsed @ 17 mths; recovered to poor health; working.
272	M	20	7 dys	Fit c/o headaches	B 2 T 30	9 wks		10 mths	C 5 Ts-	20 mths.	Excellent recovery
276	M	20	3 wks	No wasting but too weak to walk.	B 2 T29	6 wks	T15	10 mths	C 10 Ts-	20 mths	Excellent recovery

277	M	35	2 mths	Weak, thin, able to walk	B 3 T 17	8 wks	T 15	5 mths 17 "	C 80 Ts- C 40 Ts-	19 mths	Slow recovery 2nd T. course @ 4 mths, improvement, now fit.
278	M	20	3 mths	Weak, no wasting, walks well	B 3 T 24	6 wks	B3 T29	13 " 18 " 19 "	C480 Ts+ C780 Ts++ C500 Ts- (Blood Ts +)	16 mths	Improved slowly, remains in fair health and working but tryps recur in blood & C.S.F. despite treatment.
279	M	49	1 mth	Weak, no wasting, able to walk	Fo.12	10 "	T20	10 " 17 "	C 310 Ts- C 420 Ts-	19 mths	Excellent recovery; relapsed @ 9 months; recovered remains fit and working.
289	M	30	3 mths	Wasted can walk slowly	B 3 T 28	10 "		8 "	C 8; Ts-	18 mths	Excellent recovery; remains well.
301	M	40	4 mths	Wasted,walks c help	B 6 T 29	7 "	T 2	3 mths	C1160 Ts-	12 mths	Recovered fair health, then gradually declined, became maniacal: Died.
302	M	35	3 mths	Wasted.can walk alone	B 6 T 31	4 "	B3 T12	13 " 17 "	C1240;Ts++ C 420;Ts-	17 mths	Rapid recovery; relapsed @ 13 mths; recovered; now fit and working.
303	M	45	3 wks	Thin,weak able to walk	B 6 T 15	2 "		3 "	C 50: Ts-	17 mths	Recovered slowly, now fit and working.
304	M	25	3 Dys	c/O Headache only	B 5 T 31	4 "		7 " 17 "	C 5; Ts- C120: Ts-	17 mths	Rapid recovery, condition now excellent clinically.
246	M	17	3 wks	Fit c/o Headache & Fever	B 4 T 30	6 "				21 mths	Excellent recovery.
305	F	35	2 mths	Emaciated,can just walk	B 6 T 30	5 "	B1 T12	.9 "	C1500 Ts+	17 mths	Reacted well and was able to work; relapsed at 9 mths;partially recovered,remains weak and listless.
306	M	40	2 mths	Weak, no wasting,walks well	B 4 T 25	6 "	B5 T12	7 "	C 50: Ts-	17 mths	Good recovery was working, relapsed @ 7 mths,regained fair health but became epileptic.
307	M	35	3 mths	Practically moribund.	B 4						No reaction; Died

308	M	25	6 Mths	Wasted:unable to stand	B 4 T 33	9 wks		7 mths	C20:Ts-	17 Mths	Rapid recovery; remains in excellent health.
309	F	35	3 Mths	Wasted & powerless	B 1					2 dys	No reaction ; Died.
310	F	55	3 Mths	Wasted, just able to walk	B 4 T 29	6 wks.		7 mths	C80;Ts-	10 mths	Regained fair health, gradually declined; Died.
314	M	25	8 Mths	Wasted,unable to walk alone	B 9 T 17	6 wks				14 mths	Reacted badly; remains thin and weak.
318	M	20	6 wks	Thin;walks briskly	B 7 T 28	8 wks		4 mths 14 mths	C50: Ts- C140:Ts-		Good recovery; now apparently fit and working.
320	F	25	4 mths	Emaciated & powerless	B 2					2 dys	No reaction ; Died.
321	M	30	1 mth	Outwardly fit,feverish	B 9 T 19	3 wks				14 mths	Rapid recovery; remains fit.
322	M	40	2 Mths	Emaciated & powerless	B 5			D	C20 Ts-	2 wks	No recovery; Died.
323	M	25	2 Wks	Fit: c/o headaches only	B 5 T 47	6 wks		4 mths 12 mths	C90; Ts; C90; Ts-	14 mths	Excellent recovery.
326	M	15	3 mths	Good condition. C/o weakness	B 3 T 15	4 wks	T8	10 mths	C80; Ts-	14 mths	Good recovery; relapsed at 9 mths, now in fair health and working.
327	M	60	8 Mths	Weak,thin but able to work	B 5 T 25	5 wks	T8	3 mths 6 mths	C140:Ts- C470:Ts-	9 mths	Recovered fair health; relapsed at 6 months, gradually weakened; Died
328	F	13	1 mth	Emaciated can walk slowly	B 5 T 21	5 wks	B5	4 mths 8 mths	C50: Ts- C350:Ts+++		Remained weak and listless, just able to walk, gradually declined; Died
332	M	18	5 wks	Wasted,unable to stand	B 5 T 30	6 wks	B2 T11	2 mths 8 mths	C 8 ;Ts- C340;Ts-	12 mths	Rapid recovery, relapse at 8 mths, recovered now fit and working

333	M	30	2 Mths	emaciated, powerless	B6 T7			1 mth	C1160 Ts-	2 mths	No recovery; Died.
334	M	25	4 Days	Excellent condition. C/o pains in neck	B7 T14	4 wks		D 8 mths	C 8 Ts- C 8 Ts-	12 mths	Excellent recovery.
336	F	35	8 wks	Thin, walks briskly	B3 T21	7 wks				12 mths	Steady recovery, remains in fair health.
337	M	20	6 wks	Emaciated, just able to walk	B2 T19	7 wks				12 mths	Good reovery; remains fit and working.
341	M	35	3 wks	Good condition	B 3 T13	15 days		1 mth 8 mths	C4: Ts- C80:Ts-	11 mths	Excellent recovery.
342	M	30	7 dys	Weak, no wasting, can walk slowly	B4 T13	15 dys		3 wks 8 mths	C5: Ts- C200:Ts-	11 mths	Good recovery; remains in fair health, working, 11 mths Blood+ no symptoms
343	M	35	20 dys	Good condition, working	B4: T13	15 days	T.13	1 wk 9 mths	C 5: Ts- C189: Ts-	11 mths	Rapid recovery; some headaches at 10 mths., treated andd now remains fit.
344	F	18	3 mths	Wasted, unable to stand	B3: T13	15 dys		D	C250:Ts-	2½mths	Poor reaction: Died.
361	M	30	8 wks	Thin, weak, walks well	B4 T15	15 days		D 9 mths	C 10: Ts- C 7: Ts-	9 mths	Rapid recovery; remains fit.
362	M	20	8 dys	Good condition; working	B4 T15	15 days		3 wks	C50: Ts-	8½mths	Rapid recovery; remains fit.
363	M	25	5 mths	Moribund	B4:			D	C20; Ts+++	10 days	No recovery; Died.
364	M	15	6 wks	Thin, walks well	B4:	4 wks		5 mths	C150 Ts-	8 mths	Recovered fair health.
365	M	50	3 mths	Weak, wasted, just able to walk	T 18						Blood became + and diagnosis made one day before death.
367	M	20	14 dys	Good condition, working	B4: T5	4 dys		2 wks 4 mths	C20: Ts- C40: Ts-	6 mths	Treatment incomplete: remains in good health
368	M	14	1 dy.	Good condition, feverish	B3 T9	15 dys		D	C120:Ts-	6 mths	Excellent recovery
369	M	8	2 wks	Thin, weak, able to walk	B3: T11	21 dys				6 mths	Excellent recovery

370	M	3½	4 dys	Apparently fit c/o Constipation	B 1 T3½	15 Dys				6 Mths	Excellent recovery.
371	M	45	3 Dys	Good condition; c/o weakness	B4 T15	15 Dys		D 3 Mths	C780: Ts- C 80: Ts-	6 Mths	Recovered good health; remains fit.

Note:- Treatment and Observation of the following (1927) cases are incomplete :-

374	F	18	Dys	Thin; weak ; walks well	B3 T13	15 Dys		D 3 Mths	C 35: Ts- C150: Ts+	5 Mths	Recovered fair health; was working when C.S.F found+
375	M	10	Mths ?	"Healthy Carrier"	B.1: T 1.8	15 Dys				5 Mths	Remained fit; Blood became positive again in 5 Mths.
376	M	13	?3 Dys	Thin, weak, able to walk	B3: T5	10 Dys		D	C260: Ts-	4 Mths	Slow recovery to fair health.
377	F	35	6 Wks	Weak, no wasting	B3 T15	15 Dys		D	C20: Ts-	3 wks	No recovery; Died.
378	M	25	4 Mths	Moribund	B3 T7	5 Dys		D	C150: Ts-	2 wks	Remained comatose: Died.
379	M	18	?6 Dys	No wasting: C/o paresis of legs. Unable to stand	B4: T15	15 Dys		D	C140: Ts+	4 Mths	Rapid improvement, now apparently fit.
380	F	30	?11 Dys	No wasting; Condition fair	B4: T13	15 Dys		1 wk.	C160: Ts-	4 Mths	Poor reaction; became delirious now weak and listless.
381	M	50	7 wks	Emaciated; just able to walk	B4: T7	5 Dys		1 mth	C20: Ts-	1 Mth	Reacted badly; got Dysentery; Died.
382	M	45	10 Dys	Thin, weak, able to walk	B4 T15	15 Dys		D	C40 Ts-	3 Mths	Good recovery; remains fit.
383	M	14	7 Dys	c/o body pains only.	B3 T10	15 Dys		D	C150 Ts-	3 Mths	Do. Do.
385 391	M	25	2 Dys	Stuporose, otherwise fit.	B3 T15	15 Dys		D	C150 Ts-	3 Mths	Do. Do.

391	F	35	6	wks	Practically moribund	B4			D	C179:Ts+	6 Dys	No reaction ; Died
392	M	40	7	wks	Emaciated, can walk c help.	B4 T11	11 Dys		D	C60: Ts+	1½ Mths	Poor reaction.
393	M	25	3	wks	Stuporose, slight wasting	B2			D	C85: Ts-	3 Dys	No reaction: Died.
394	M	25	3	wks	Thin,wasting	Course not com :plete			D	C480 Ts+++	----	
395	F	25	3	wks	No wasting, c/o weakness, able to walk	Do.			D	C540 Ts++	----	
396	M	30	2	mths	Good condi-tion	Do.					------	

APPENDIX B.

Extracts from Charts.

Case 180. Illustrates the lack of relationship between pulse rate and temperature, also the persistent pyrexia during treatment which is a bad prognostic sign.

Case 267. To show the tachycardia gradually settling down after specific treatment.

Case 371. Illustrates a normal reaction after 'Bayer' and the steadying effect of that drug on the pyrexia of an early case.

Case 381 Subnormal temperature in an advanced case. There is no reaction to 'Bayer', but the pyrexia of a late complication is shown followed by the subnormal temperature of the terminal stupor.

Case 306. Chart of a clinical relapse occurring 7 months after cessation of previous treatment. It shows the effect of 'Bayer' on the pyrexia but this was only temporary the patient subsequently becoming epileptic.

Case 318. Illustrates the incomplete action of 'Bayer', a rise of temperature 12 days after injection indicating the return of trypanosomes to the peripheral blood.

= = = = = = = = = = = = = = =

DISEASE.

TRYPANOSOMIASIS

RHODESIENSIS

Notes of Case.

Name { KAYOYULE.

Age 20

Diet

Case Book No. 180

Previous Treatment

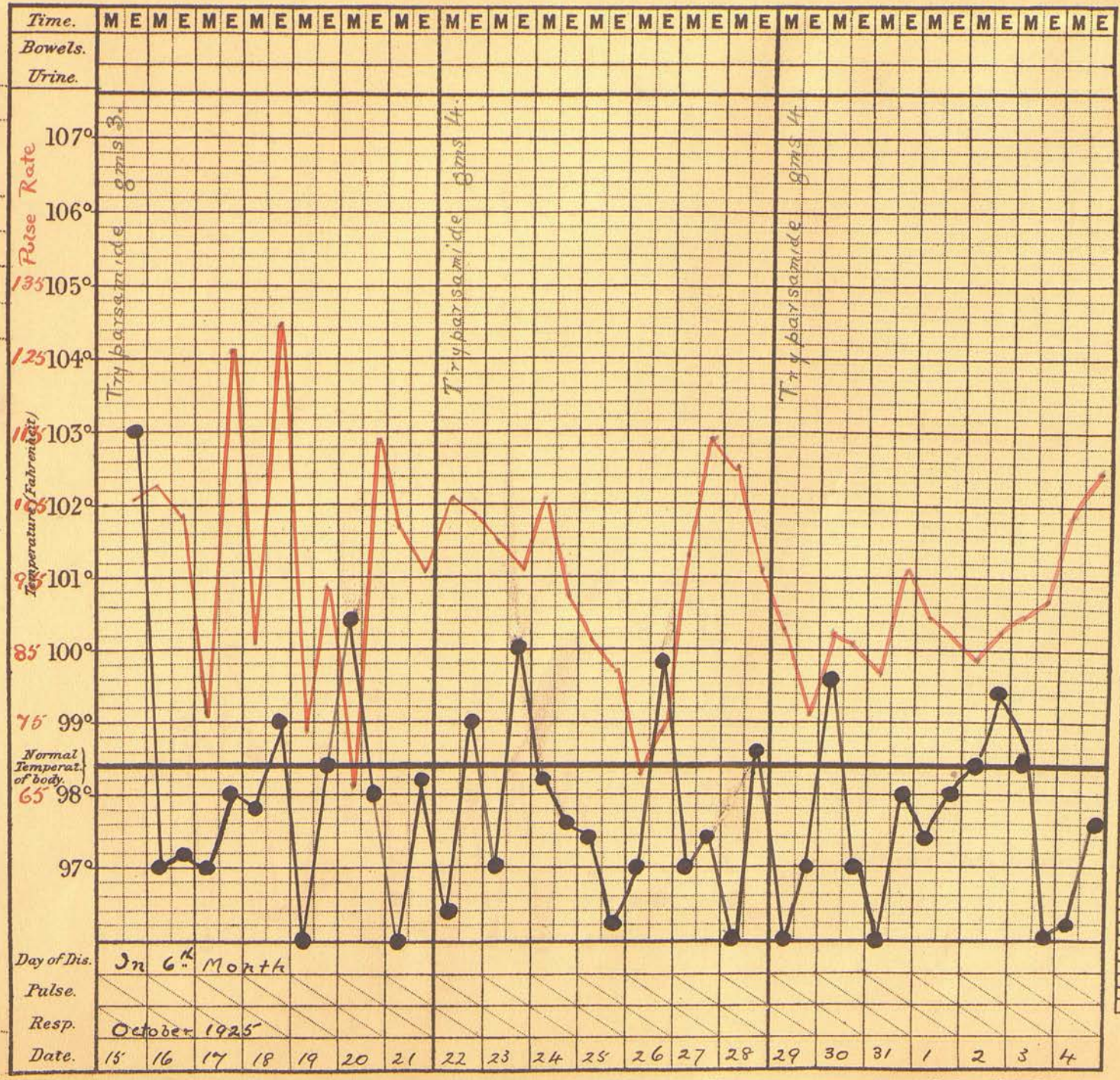
Bayer gms 2

Tryparsamide gms 13

Date of admission.

20 - 9 - 25

Result DIED



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DISEASE.

TRYPANOSOMIASIS RHODESIENSIS

Notes of Case.

Name { Meri

Age 40

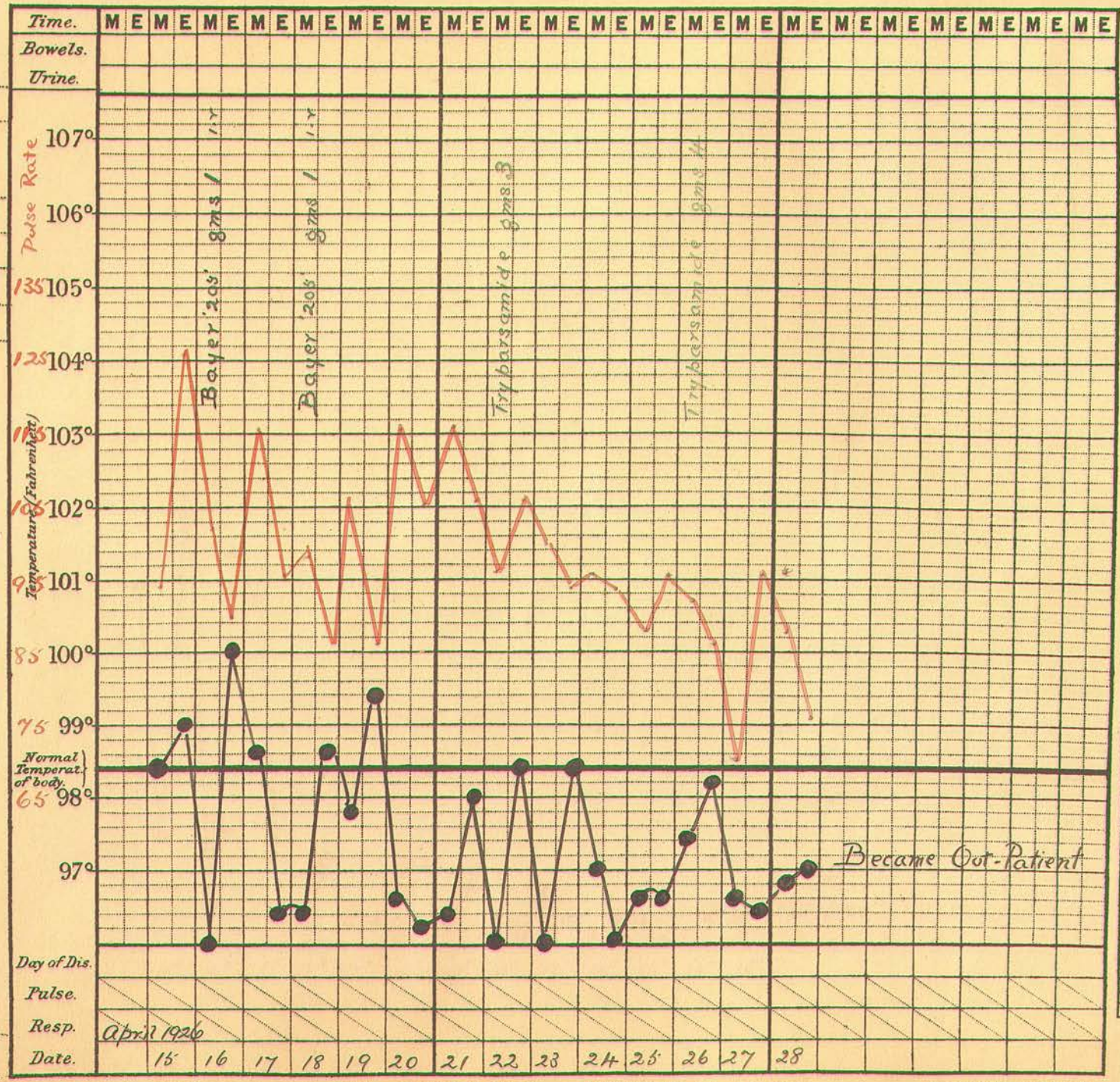
Diet

Case Book No. 267

Diagnosed 15th 4.26
Blood. Positive

Date of admission.
15 - 4 - 26

Result Recovered



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DISEASE.

TRYPANOSOMIASIS RHODESIENSIS

Notes of Case.

Name MANYOTA

Age 45

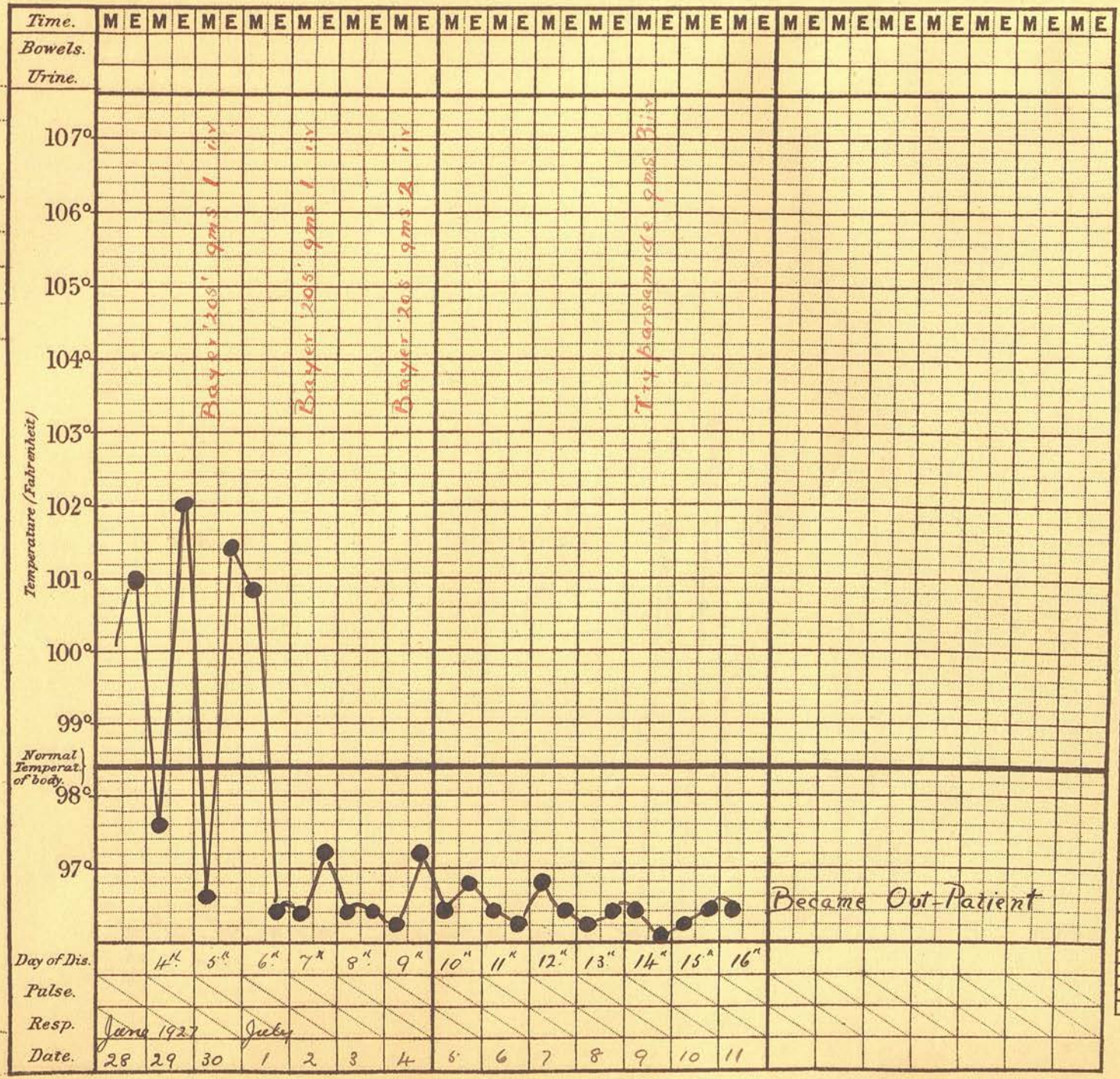
Diet

Case Book No. 371

Diagnosed 29.6.27
Blood Positive

Date of admission.
28 - vi - 27

Result Recovered



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DISEASE.

TRYPANOSOMIASIS RHODESIENSIS

Notes of Case.

Name SELIMANI

Age 50

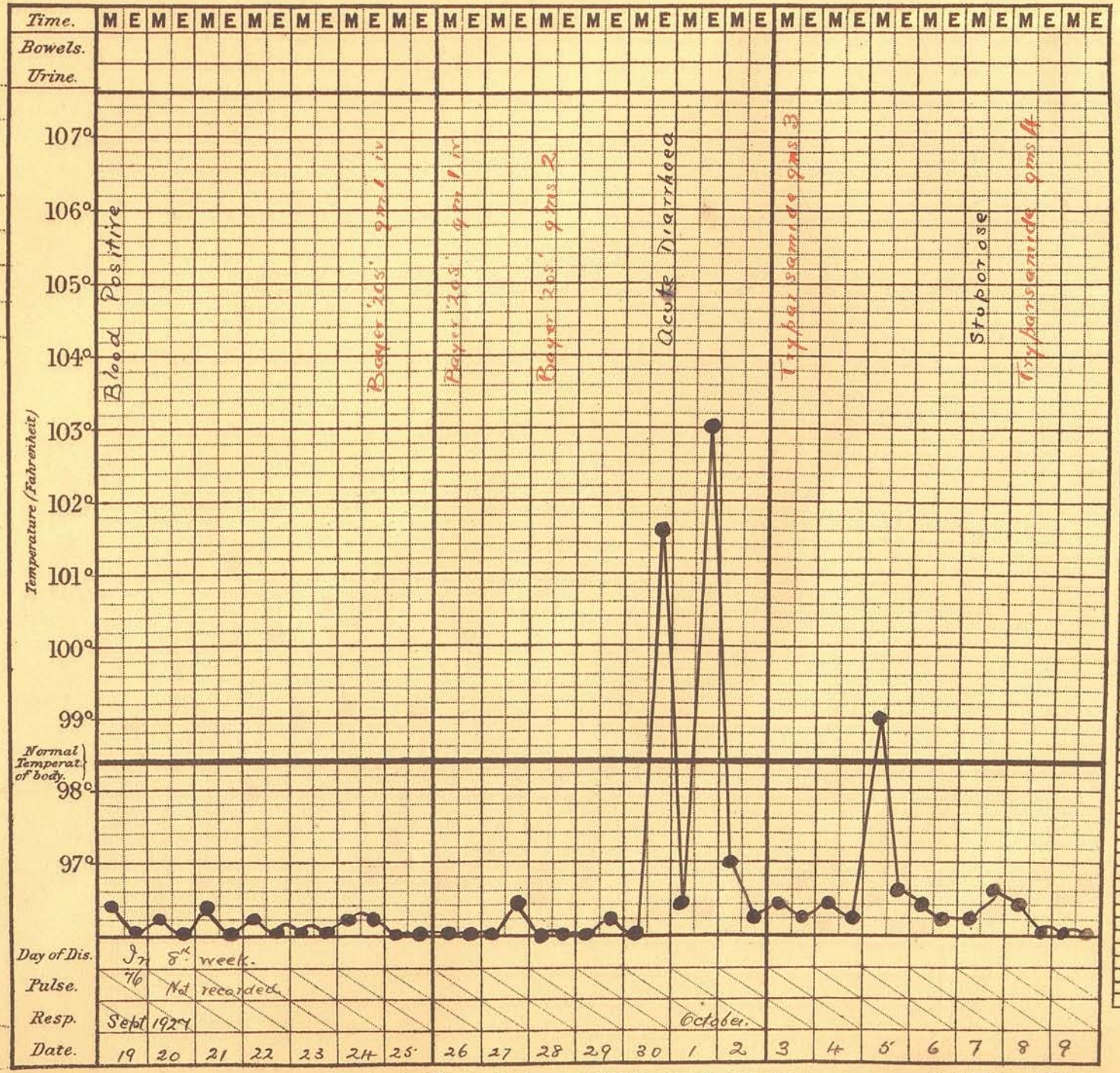
Diet

Case Book No. 381

Diagnosed 19-9-27
Blood Positive

Date of admission.
19th Sept 1927

Result DIED



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DISEASE.

TRYPANOSOMIASIS RHODESIENSIS

Notes of Case.

Name PIGANGOMA

Age 40

Diet

Case Book No. 306

1st Relapse. 27·4·27.

c/o headache and fainting fits

Blood neg.

C.S.F. neg.

— — — — —

Previous Treatment

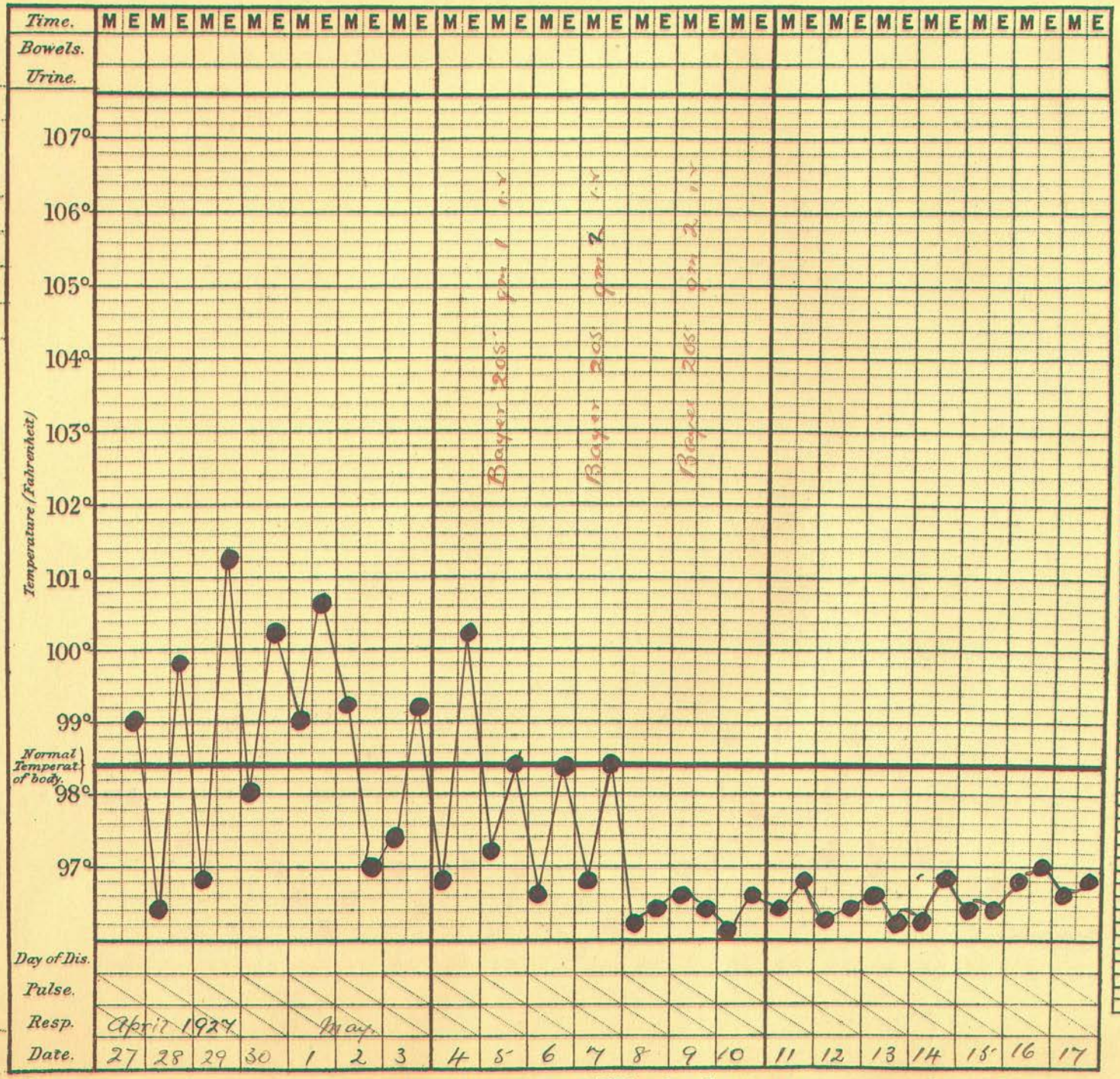
Bayer 4 gms

Tryparsamide 24 gms

Date of admission.

27th July 1926

Result Uncured.



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DISEASE.

TRYPANOSOMIASIS RHODESIENSIS

Notes of Case.

Name Majiaskamba

Age 25

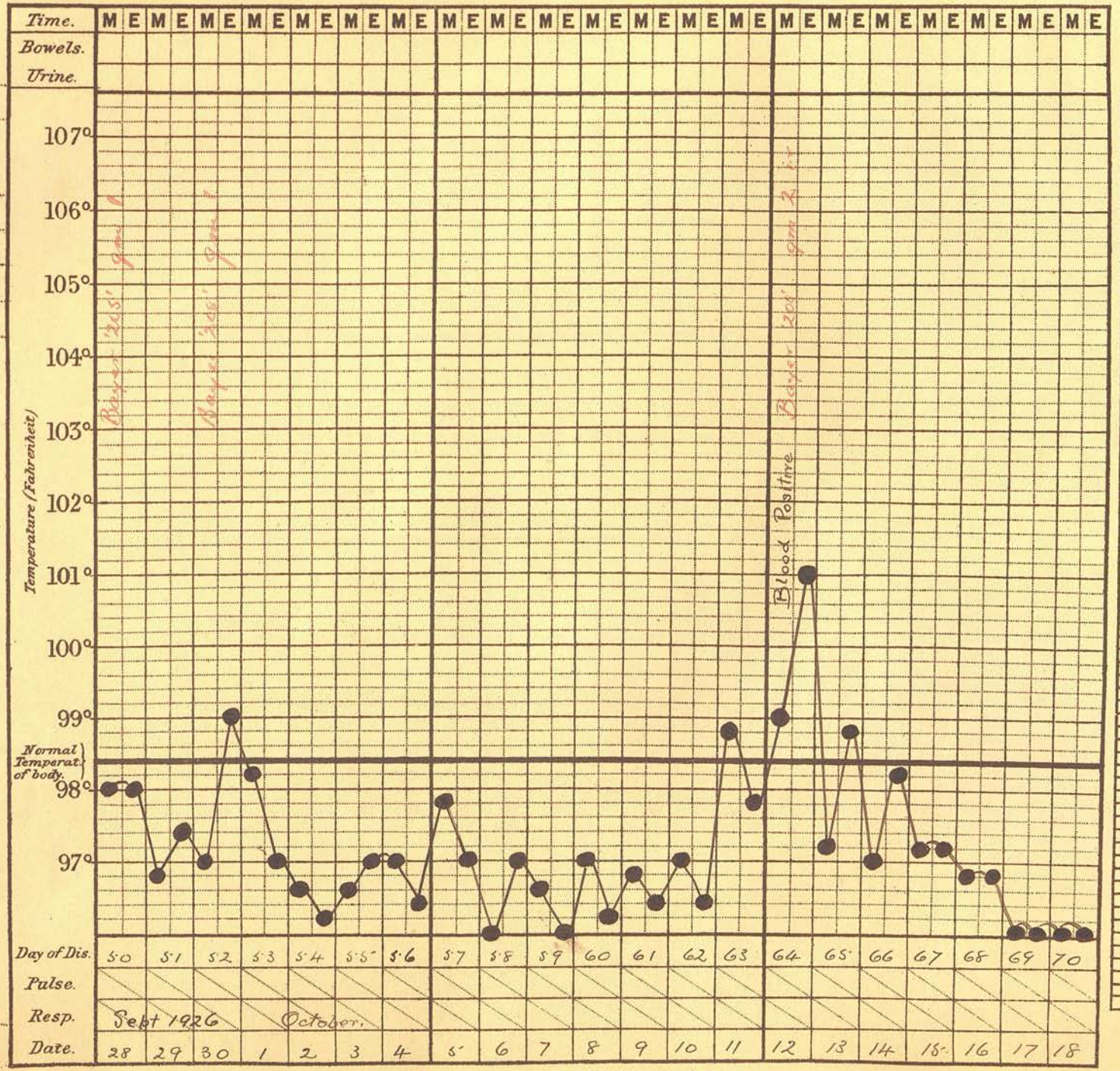
Diet

Case Book No. 318

Diagnosed 28-9-26
Blood Positive

Date of admission.
26th Sept 1926

Result Cured.



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APPENDIX C.

Trypanosomes in Game.

1) Examinations of Peripheral Blood.

Animal	Number Examined	Positive	Negative
Waterbuck	33	18	15
Impala	19	1	18
Topi	17	3	14
Zebra	24	2	22
Eland	13	4	9
Roan	5	0	5
Bushbuck	5	1	4
Hartebeeste	6	0	6
Giraffe	5	1	4
Sable	2	0	2
Warthog	5	0	5
Elephant	2	0	2
Puku	5	1	4
Hippopotamus	1	0	1
Leopard	1	0	1
Hyaena	2	0	2
Reedbuck	2	0	2
Buffalo	1	0	1
Crocodile	2	0	2
TOTALS	150	31	119

2) Classification of the Trypanosomes.

Note: The trypanosomes are classified according to main types and finer distinctions of species are not recorded in this table.

Animal	N°.	Diagnosis	Total	Remarks
Waterbuck Eland Bushbuck Puku	8 2 1 1	T. *brucei*	12	
Waterbuck Eland Topi Giraffe Impala	3 1 1 1 1	T. *vivax*	7	
Waterbuck Eland	2 1	?T. brucei or a mixed *brucei* and *vivax* infection.	3	Many typical *vivax* present but also a number of polymorphic *brucei* forms
Zebra	1	T. *congolense*	1	
Waterbuck Topi	2 1	?T. *brucei*	3	Tryps. scanty but correspond to *brucei* type.
Waterbuck	2	?T. *vivax*	2	Very scanty tryps. correspond to *vivax* type.
Waterbuck Topi Zebra	1 1 1	Doubtful	3	Only very scanty tryps. morphology quite uncertain.

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